REMARKS

Applicants request reconsideration of the above-identified application in view of the foregoing amendments and following remarks.

Applicants have amended the specification to update the priority information.

Applicants have cancelled claims 1-6 and presented new claims 34-37. Support for claim 34 can be found, for example, in originally filed claims 1-3 as well as on page 15, lines 4 to 21 of the specification. Support for claim 35 can be found, for example, in originally filed claim 4 as well as on page 16, lines 10 to 16 of the specification. Support for claims 36 and 37 can be found, for example, in originally filed claims 5 and 6.

Claims 7-33 were previously cancelled as drawn to non-elected subject matter.

None of the new claims presents new matter. Any cancellation of claims or subject matter are made without waiver of applicants' rights to continue to prosecute and obtain claims directed to the former subject matter either in this application or in other applications.

Thus, claims 34-37 are pending in this application.

The Rejections

35 U.S.C. § 112, Second Paragraph: Indefiniteness

Claims 1 and 4-6 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. Each part of the rejection is discussed separately below.

The Examiner contends that claim 1 is rejected as there is no function assigned to the "functional fragment" of PAMP (claim 1). Applicants traverse to the extent that the rejection applies to claim 34.

Claim 34 is drawn to an isolated human, mouse or *D. melanogaster* PAMP, or a *function-conservative fragment* thereof. As defined in the specification, a function-conservative fragment is one in which a given amino acid residue in a protein has been changed without altering the overall conformation and function of the polypeptide (see page 15, lines 4 to 21 of the specification). With respect to PAMP functions, the specification teaches, for example, several potential functions

of PAMP based on the identification and characterization of several PAMP sequence motifs (see section entitled "PAMP" on page 7, line 5 to page 9, line 23). The specification additionally teaches PAMP's function and role in ßAPP processing and *Notch/Glp1* transduction (see Examples 1 and 2). In light of the teachings of the specification, it would be clear to one of ordinary skill in the art that a function-conservative fragment refers to any PAMP fragment which retains a function attributed to full-length PAMP.

Claim 4 stands rejected as referring to a mutant PAMP, for which there is no antecedent basis in claim 1. The Examiner suggests that applicants make claim 4 an independent claim.

Following the Examiner's suggestion, applicants have cancelled claim 4 and presented independent claim 35, drawn to PAMP mutants which are substantially homologous to human, mouse or *D. melanogaster* PAMP.

Claim 5 stands rejected because it is allegedly unclear what the biochemical changes similar to mutations in PS1, PS2, or β-amyloid are. Applicants traverse the rejection to the extent that it applies to claim 36.

As disclosed throughout the specification, PAMP mutants may cause biochemical changes (similar to those associated with mutations in PS-1, PS-2, or β-APP) which affect the onset or progression of Alzheimer's Disease (page 19, lines 10-25; Example 2). Such changes include, but are not limited to, changes in β-catenin translocation (page 18, lines 28-30) changes in the γ-secretase mediated βAPP processing (Example 1 at page 34, lines 30-35), and changes in $A\beta_{42}$ and $A\beta_{40}$ peptide levels and $A\beta_{42}/A\beta_{40}$ ratio (Example 2 at page 38, lines 22-32). Thus, in light of the specification, the metes and bounds of the term "biochemical changes" would be apparent to one of skill in the art.

Claim 6 stands rejected as allegedly having no reference sequence identification number for the mutations listed.

Applicants have canceled claim 6 and substituted therefor claim 37 which recites "human PAMP (SEQ ID NO:14)" thus obviating the Examiner's rejection.

In light of the amendments and arguments presented above, applicants request that the Examiner withdraw the pending 35 U.S.C. § 112, second paragraph rejections.

35 U.S.C. § 102(a) and 35 U.S.C. § 103(a)

Claims 1, 3 and 4 stand rejected under 35 U.S.C. 102(a) as allegedly being anticipated by or being unpatentable under 35 U.S.C. 103(a) by the *C. elegans* Sequencing Consortium ("Consortium"). The Examiner states that the Consortium teaches an amino acid sequence that shares 99.7% identity to SEQ ID NO: 12 and that the instant specification (page 34, para. 1) teaches that this *C. elegans* homologue of PAMP is identical to the sequence disclosed by the Consortium. Thus, the Examiner states, the teachings of the Consortium anticipate or render obvious claims 1 and 3. The Examiner has also rejected claim 4 as "one PAMP can be considered to be a mutant of the PAMP of another species; thus, the *C. elegans* PAMP is a mutant of the human, mouse, and Drosophila PAMP, for example." Additionally, according to the Examiner, the *C. elegans* PAMP would be considered to comprise a functional fragment of the human, mouse, and Drosophila PAMP. The Examiner also states that claim 2 is objected to for being dependent upon a rejected claim but would be allowable if rewritten in independent form. Applicants traverse.

In the context of former claims 1, 3 and 4, the Examiner argues that the *C. elegans* PAMP would be considered to be a functional fragment or mutant of the human, mouse and *D. melanogaster* PAMP. Applicants respectfully disagree. However, solely to expedite prosecution, applicants have cancelled claims 1 and 3 and substituted therefore claim 34 drawn to isolated human, mouse or *D. melanogaster* PAMP, and *function-conservative fragments* thereof. As defined in the specification (page 15, lines 4 to 21), function-conservative variants are proteins in which a given amino acid residue in a protein or enzyme has been changed without altering the overall conformation and function of the polypeptide. The specification goes on to teach that such variants may be, for example, at least 70% similar to the native protein or have at least 60% amino acid identity to the native protein. *C. elegans* PAMP does not satisfy these limitations.

As demonstrated, the human PAMP protein has 22% sequence identity and 39% sequence similarity to the hypothetical *C. elegans* protein (Example 1, particularly page 32, lines 15-21). *C. elegans*, therefore, is not a function-conservative fragment of human PAMP as defined in this

application. As shown in the BLAST 2 Sequence Alignments attached as Exhibit A, mouse PAMP has 21% identity and 41% similarity to *C. elegans* PAMP while *D. melanogaster* PAMP has 23% identity and 41% similarity to *C. elegans* PAMP. Thus, as claim 34 does not embrace *C. elegans* PAMP and *C. elegans* PAMP is not a function-conservative fragment of human, mouse or *D. melanogaster* PAMP, claim 34 is not anticipated or rendered obvious by the Consortium sequence.

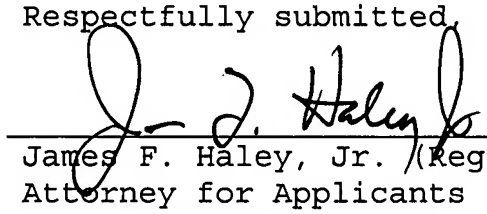
Applicants have also cancelled claim 4 and substituted therefor claim 35 drawn to PAMP mutants, and fragments thereof, which are substantially homologous to human, mouse or *D. melanogaster* PAMP. As defined in the specification (page 16, lines 10 to 16), substantially homologous mutants are those in which greater than 80% of the amino acids are identical, or greater than about 90% are similar to the wild type protein. Again, as shown in Exhibit A, *C. elegans* PAMP is not a substantially homologous mutant of human, mouse or *D. melanogaster* PAMP. Thus, claim 35 is not anticipated or rendered obvious by the Consortium sequence.

In light of the amendments and arguments presented above, applicants request that the Examiner withdraw the rejection of the pending claims.

Conclusion

Applicants request favorable consideration of the application and early allowance of the pending claims.

Respectfully submitted,



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